



**UNITED STATES DEPARTMENT OF COMMERCE
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SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
02/252,710	06/02/94	RIVIERE	1 8141113

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EXAMINER	
FREDMAN, J	
ART UNIT	PAPER NUMBER
1809	

DATE MAILED: 11/12/96

Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents

Advisory Action

Application No.

08/252,710

Applicant(s)

Riviere et al

Examiner

Jeffrey Fredman

Group Art Unit

1809



THE PERIOD FOR RESPONSE: [check only a) or b)]

- a) ☐ expires _____ months from the mailing date of the final rejection.
- b) ☒ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

- ☒ Appellant's Brief is due two months from the date of the Notice of Appeal filed on Oct 15, 1996 (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

Applicant's response to the final rejection, filed on Oct 15, 1996 has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:

- ☒ The proposed amendment(s):
- ☐ will be entered upon filing of a Notice of Appeal and an Appeal Brief.
 - ☒ will not be entered because:
 - ☐ they raise new issues that would require further consideration and/or search. (See note below).
 - ☒ they raise the issue of new matter. (See note below).
 - ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.
 - ☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: see attached sheet.

- ☐ Applicant's response has overcome the following rejection(s):

- ☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.
- ☒ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:
see attached response

- ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

- ☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: none

Claims objected to: none

Claims rejected: 1-4, 6-31, and 35-37

- ☐ The proposed drawing correction filed on _____ ☐ has ☐ has not been approved by the Examiner.
- ☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☒ Other See attached sheet regarding IDS

Attached Sheet

Information Disclosure Statement

1. The information disclosure statement filed September 13, 1996 fails to comply with 37 CFR 1.97(d) because it lacks a certification as specified in 37 CFR 1.97(e). It has been placed in the application file, but the information referred to therein has not been considered.

Response to Amendment

2. The amendment has not been entered because, under 35 U.S.C. 132, it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The discussion regarding the amendment fails to show how the specification differentiates the various sequences with their cartoon legends within the figure. For example, in the aG-SGC line of figure 11, a specific order of clear square, followed by a line followed by diagonal square, black square, stippled square, followed by a line followed by a white square is shown. There is no discussion pointing to statements in the specification which indicate which square is correlated with which DNA sequence. The MPEP 608.04(a) states "Matter not in the original specification, claims, or drawings is usually new matter. Depending on circumstances such as the adequacy of the original disclosure, the addition of inherent characteristics such as chemical or physical properties, a new structural formula or a new use may be new matter. See Ex parte Vander Wal, et al. , 1956 C.D. 11; 705 O.G. 5 (physical properties), Ex parte Fox , 1960 C.D. 28; 761 O.G. 906 (new formula) and Ex parte Ayers, et al. , 108 USPQ 444 (new use)." For these reasons, the amendment is not being entered since new matter considerations are involved.

Response to Declaration

3. The Declaration under 37 CFR 1.132 filed October 15, 1996 is insufficient to overcome the rejection of the claims based upon 35 U.S.C. 103 as set forth in the last Office action because:

The Declaration states that subsequent studies showed that the retroviral titers of Cone were insufficient to effectively transduce mammalian cells without selection and cites the Jaffee reference to support this assertion. No specific statement was found in the Jaffee reference indicating the titer of the retrovirus used. This reference, therefore, provides no evidence regarding the lack of reasonable expectation of success.

A second point regarding this argument relates to the differing methodologies utilized between the Jaffee and Cone references. The Jaffee reference transduces using 5×10^5 tumor explant cells and 10 mls of the retrovirus solution (no titer is given) (page 2222, column 1, paragraph 4). The Cone reference transduces using 1×10^5 cells with titers as high as 2×10^5 cfu/ml (page 6349, column 2, paragraph 4 and page 6350, column 2, paragraph 3). Thus, from the evidence in the papers, it is unclear whether the tenfold difference in the titer stated by the Declaration to be the minimal effective titer in fact relates to true differences in titer, or is simply related to the Jaffee use of 10 mls and the Cone use of 1 ml of virus.

The next argument in the declaration relates to the time period after Cone was published. Contentions that the references are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977).

The Declaration, therefore, is given some weight in determining the obviousness of the claims. It is insufficient, however, because no factual evidence of a direct comparison between Cone and the invention is presented.

Response to Arguments

4. Applicant's arguments filed October 15, 1996 have been fully considered but they are not persuasive.

The first argument is that there is no expectation of success for the combination of the cited references. This argument is supported by an argument that seven years elapsed between Cone and the present application.

As noted above, the age of the references is not significant absent a showing of failure to solve the problem. The argument relating to the absence of a reasonable expectation of success is further weakened when one notes that Cone expressly states that success is expected "These titers are high enough to facilitate the nonselective introduction of genes into 100% of a population of cells at high enough cell numbers to allow rapid analysis of DNA, RNA, or protein (page 6353, column 1, paragraph 2)". Such an express statement that success would be expected meets the requirement of a reasonable expectation of success. The MPEP 2143.02 states

"Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art

steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991) (In the context of a biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); *In re O'Farrell*, 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.). “

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Cone reference of the enabling methodology, the suggestion to modify the prior art, and a statement that the modification would be successful. The statement that Cone is wrong is not based on a factual analysis of the Cone reference as noted in the response to the Declaration above and is an unsupported assertion.

The next argument relates to the unobviousness of the problem solved by applicant. As noted in the previous response, specific motivation is present to make the claimed invention. Further, the MPEP 2144 states “The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).” In this instance, there is suggestion to combine the references and it need not solve applicant's problem.

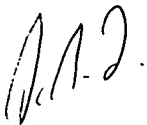
For the reasons given above as well as those stated in the final rejection, the rejections are maintained.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeff Fredman, Ph.D. whose telephone number is (703) 308-6568.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 180 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center number is (703) 305-7401. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).



Jeffrey Fredman, Ph.D.

November 7, 1996



GEORGE C. ELLIOTT
PRIMARY EXAMINER
GROUP 1800